Global Mapping of XAS Data: Structure of the Active Site of Cobalamin Enzymes

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The two available crystallographic structures of cobalamin dependent enzymes, the 27 kDa fragment of the methylcobalamin-dependent enzyme, methionine synthase, from *Escherichia coli* [C.L. Drennan *et al*. *Science*, **266**, 1669 (1994)] and the 5'-deoxyadenosylcobalamin-dependent enzyme methylmalonyl-coenzyme A mutase from *Propionibacterium shermanii* [F. Mancia *et al*. *Structure*, **4**, 339 (1996)], show striking similarities despite the differences in reaction mechanism. In particular, the 5,6-dimethylbenzimidazole group is detached and replaced by a histidine group of the enzyme. We have analyzed Extended X-ray Absorption Fine Structure (EXAFS) spectroscopic data for both 5'-deoxyadenosylcobalamin and aquocobalamin bound to methylmalonyl-coenzyme A mutase in the absence of substrate. The analysis is conducted with a suite of programs called AUTOFIT 1.0 [Chance *et al*., *Biochemistry*, 1996, ***35*,** 9014], which allows an evenhanded comparison of the goodness-of-fit of the EXAFS data to a varied grid of simulations based on the *ab initio* EXAFS code FEFF 6.01. The x-ray edge data indicate an increase in effective nuclear charge of the metal ion of the enzyme bound 5'-deoxyadeonsylcobalamin compared to the corresponding free cobalamin and the EXAFS results show small decreases in equatorial and no significant change in the Co-C bond length.